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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 09/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/864,291	OKO ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 6/11/04

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-67 and 69-74* is/are pending in the application.

4a) Of the above claim(s) *1-7,16-47,49-52,54-59,63,64 and 69-72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,9,11-15,48,53,60-62,65-67 and 73* is/are rejected.

7)☒ Claim(s) *10 and 74* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-67 and 69-74 are pending.

Applicants' amendment filed June 11, 2004 is acknowledged. Applicant's response has been considered. Claims 8-11, 13, 15, 48, 61, 62 and 67 have been amended, claim 68 has been cancelled, and new claims 73 and 74 have been added. Claims 1-7, 16-47, 49-52, 54-59, 63, 64 and 69-72 are non-elected inventions and stand withdrawn from consideration. Therefore, claims 8-15, 48, 53, 60-62, 65-67, 73 and 74 are examined.

This application contains claims 1-7, 16-47, 49-52, 54-59, 63, 64 and 69-72 drawn to an invention nonelected with traverse in the response to the restriction requirement filed November 14, 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

2. The foreign priority document of Canada Application 2307128 submitted June 11, 2004 is acknowledged.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

3. The previous rejection of claims 9, 10, 48 and 67, under 35 U.S.C.112, second paragraph, is withdrawn in view of applicant's amendment to the claim, and applicants' response at pages 13-14 of the amendment filed June 11, 2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 8, 9, 11-15, 48, 53, 60-62, 65-67 and 73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide sequence of SEQ ID NO:4 or 11, or a polynucleotide encoding a polypeptide comprising the sequence of SEQ ID NO:5 or SEQ ID NO:12; a gene or a vector comprising the polynucleotide; a host cell comprising the vector; or a method of producing the polypeptide, does not reasonably provide enablement for a polynucleotide comprising a sequence that hybridizes to the sequence of SEQ ID NO:4 or 11 under a cited hybridization condition and encodes a polypeptide having the activity of inducing oocyte activation, a gene or a vector comprising the polynucleotide, a host cell comprising the vector, and a method of producing the polypeptide; or a polynucleotide comprising a sequence that is at least 75% identical to nucleotides 36 to 975 of SEQ ID NO:4 or to nucleotides 1 to 705 of SEQ ID NO:11, wherein the polynucleotide encodes a polypeptide having an activity of inducing oocyte activation, but the polynucleotide sequence is not defined. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 8, 9, 11-15, 48, 53, 60-62, 65-67 and 73 are directed to a polynucleotide comprising a sequence of SEQ ID NO:4 or 11 or a sequence that hybridizes to the sequence of SEQ ID NO:4 or 11 and encodes a polypeptide having the activity of inducing oocyte activation (claims 73, 8, 9, 48, 53, 60 and 65-67), a gene (claim 11) or a

vector (claims 12, 13) comprising the polynucleotide, a host cell comprising the vector (claim 14), and a method of producing the polypeptide (claim 15); or a polynucleotide comprising a sequence that is at least 75% identical to nucleotides 36 to 975 of SEQ ID NO:4 or to nucleotides 1 to 705 of SEQ ID NO:11, wherein a polypeptide encoded by the polynucleotide induces oocyte activation (claims 61 and 62). The specification, however, only discloses cursory conclusions (pages 4-10) without data supporting the findings, which state that the present invention features perinuclear theca polypeptide comprises at least one of PPPGY and LPPAY, and at least three domains having the sequence of YGXPPXG, or, the polypeptide comprises the sequence of PPXY, and at least three domains having the sequence of YGXPPXG, these polypeptides include bovine or human PT32 or biologically active fragment thereof; and the polynucleotides encode the polypeptides. There are no indicia that the present application enables the full scope in view of the polynucleotides comprising a sequence that hybridizes to the sequence of SEQ ID NO:4 or 11 and encodes a polypeptide having the activity of inducing oocyte activation, and a polynucleotide variant of SEQ ID NO:4 or 11 as discussed in the stated rejection. The present application does not provide sufficient teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the presence or absence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the polynucleotide comprising a sequence that hybridizes to the sequence of SEQ ID NO:4 or 11 under a cited hybridization condition and encodes a polypeptide having the activity of inducing oocyte activation; or the polynucleotide comprising a sequence that is at least 75% identical to nucleotides 36 to 975 of SEQ ID NO:4 or to nucleotides 1 to 705 of SEQ ID NO:11 and encoding a polypeptide having the activity of inducing oocyte activation, which are not adequately described or demonstrated in the specification.

(2). The presence or absence of working examples:

The specification indicates the PT32 cDNA sequence has been identified, the rPT32 has been produced, and the injection of rPT32 into cytoplasm of bovine oocytes yield rates of oocyte activation that were similar to the rate of activation injected with perinuclear theca extracts (Table 1, pages 64-78). However, there are no other working examples indicating the claimed variants except for the polynucleotide sequence of SEQ ID NO:4 or 11. Figs. 7A-7E show RNA obtained from various tissues probed with PT32 anti-sense RNA, it appears that these RNA sequences hybridize to the complement (anti-sense) of the coding sequence of PT32.

(3). The state of the prior art and relative skill of those in the art:

The related art (references shown at pages 1-4 of the specification) indicates the perinuclear theca (PT), a cytoskeletal coat of the mammalian sperm nucleus, harbors the oocyte activating factors and provides a mechanism for the release of oscillogens from the sperm head into oocyte cytoplasm at fertilization. However, the general knowledge

and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on identities of polynucleotides that hybridizes to the sequence of SEQ ID NO:4 or 11 and encodes a polypeptide having the activity of inducing oocyte activation, or polynucleotides which are variants or fragments of SEQ ID NO:4 or 11 and encode a functional polypeptide to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass many polynucleotides that hybridize to the sequence of SEQ ID NO:4 or 11 and encode a functional polypeptide; and polynucleotides that are fragments or variants of SEQ ID NO:4 or 11 and encode a functional polypeptide, but the identities of these polynucleotides are not disclosed in the specification. Since SEQ ID NO:4 or 11 is the coding sequence of PT32, it is not predictable whether the polynucleotides that hybridize to the sequence of SEQ ID NO:4 or 11 can encode a functional polypeptide.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed a polynucleotide comprising a sequence of SEQ ID NO:4 or 11 or a sequence that hybridizes to the sequence of SEQ ID NO:4 or 11 and encodes a polypeptide having the activity of inducing oocyte activation; or a polynucleotide comprising a sequence that is at least 75% identical to nucleotides 36 to 975 of SEQ ID NO:4 or to nucleotides 1 to 705 of SEQ ID NO:11, and the polynucleotide encoding a functional polypeptide. The specification indicates the PT32 cDNA sequence has been identified, the rPT32 has been produced, and the injection of rPT32 into cytoplasm of

bovine oocytes yield rates of oocyte activation that were similar to the rate of activation injected with perinuclear theca extracts (Table 1, pages 64-78); and Figs. 7A-7E show RNA obtained from various tissues probed with PT32 anti-sense RNA, it appears that these RNA sequences hybridize to the complement of the coding sequence of PT32. However, there are no other working examples indicating the claimed variants except for SEQ ID NO:4 or 11. Furthermore, the specification has not identified any polynucleotide that hybridizes to the sequence of SEQ ID NO:4 or 11 and encodes a polypeptide having the activity of inducing oocyte activation; or the polynucleotide variant that is at least 75% identical to nucleotides 36 to 975 of SEQ ID NO:4 or to nucleotides 1 to 705 of SEQ ID NO:11 and encodes a functional polypeptide. Since the specification does not provide sufficient teachings on the identities of polynucleotide sequences encoding a functional polypeptide, it is necessary to have additional guidance and to carry out further experimentation to identify various polynucleotide sequences that encode a functional polypeptide.

(6). Nature of the Invention

The scope of the claims includes many polynucleotide sequence variants, however the specification has not identified the polynucleotides encoding functional PT32 polypeptides, nor has demonstrated the effects of the PT32 variants or fragments. Thus, the disclosure is not enabling for reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed variants, and the teaching in the specification is limited, therefore, it is necessary to have additional guidance and to carry out further

experimentation to identify various polynucleotide sequences that encode a functional polypeptide.

In response, applicants indicate that claims 8, 48 and 53 have been amended to depend from new claim 73, which defines a polynucleotide comprising a sequence of SEQ ID NO: 4, SEQ ID NO:11, or a sequence that hybridizes to SEQ ID NO: 4 or SEQ ID NO:11 under defined hybridization conditions, wherein the polynucleotide encodes a polypeptide that induces oocyte activation; PT-32 is shown in Figures 7A, 7B and 7C to selectively hybridize with nucleic acids obtained from bull, human, and rat testis, identifying similar sequences across species boundaries; additional supportive data indicates that antibodies produced from PT-32 selectively recognize sperm from Rhesus monkey (Figure 6), bull (Figure 5), and human (see paragraph [0170], page 68) again indicating biological recognition of PT32 across species boundaries; microinjection of recombinant PT-32 (rPT32) into bull oocytes (see paragraph [0182] page 69) or Rhesus monkey oocytes (see paragraph [0193], page 74) resulted in oocyte activation, thus the subject matter defined in claim 73 is proper; and the nucleotides specified in claims 61 and 62 refer to the nucleotides that encode the open reading frames of the sequences defined by either SEQ ID NO:4 or 11, and claims 61 and 62 have been amended to further define the conditions for determining % identity and to indicate that the polynucleotide encodes a polypeptide that induces oocyte activation, thus, the subject matter of claims 62 and 63 is also proper.

The response has been fully considered, however, the argument is not found persuasive because of the following reasons:

Regarding claim 73, SEQ ID NO:4 or SEQ ID NO:11 is the coding sequence for bovine or human PT32 protein (SEQ ID NO:5 or 12), and Figures 7A, 7B and 7C show the anti-sense RNA of PT-32 coding sequence is used to selectively hybridize with the nucleotide sequence obtained from bull, human, and rat testis, thus, the nucleotide sequences obtained from bull, human, and rat testis are the sequences that hybridize to the complement of SEQ ID NO: 4 or 11 and that encode PT32 from various species. It is not the sequence that hybridizes to SEQ ID NO:4 or 11 encode the functional polypeptide. Therefore, the nucleotide sequence that hybridizes to SEQ ID NO: 4 or SEQ ID NO:11 and encodes a polypeptide that induces oocyte activation is not enabled.

Regarding claims 61 and 62, although the method for determining % sequence identity and the polynucleotide encodes a functional polypeptide are cited in the claim, the specification does not provide sufficient written description for a genus of polynucleotide variants (see paragraph 5). Therefore, claims 61 and 62 are not enabled.

5. Claims 8, 9, 11-15, 48, 53, 60-62, 65-67 and 73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 8, 9, 11-15, 48, 53, 60-62, 65-67 and 73 are directed to a polynucleotide comprising a sequence of SEQ ID NO:4 or 11 or a sequence that hybridizes to the sequence of SEQ ID NO:4 or 11 under a cited hybridization condition and encodes a polypeptide having the activity of inducing oocyte activation, or a polynucleotide comprising a sequence that is at least 75% identical to nucleotides 36 to 975 of SEQ ID

NO:4 or to nucleotides 1 to 705 of SEQ ID NO:11, wherein a polypeptide encoded by the polynucleotide induces oocyte activation, and the sequence identity is determined using sequence comparison software BLAST. While the specification indicates the present invention provides perinuclear theca polypeptide comprises at least one of PPPGY and LPPAY, and at least three domains having the sequence of YGXPPXG, or, the polypeptide comprises the sequence of PPXY, and at least three domains having the sequence of YGXPPXG, and these polypeptides include bovine or human PT32 or biologically active fragment thereof, and the polynucleotides encoding these polypeptides (pages 4-10); and polynucleotides having at 75% or 90% identity to a polynucleotide which encodes PT32, e.g., the polypeptide of SEQ ID NO:5 or 12, which is encoded by the polynucleotide of SEQ ID NO:4 or 11 (page 22, paragraph [0055]), the specification does not disclose a genus of variants for sequence that hybridizes to the sequence of SEQ ID NO:4 or 11 under a cited hybridization condition and encodes a polypeptide having the activity of inducing oocyte activation; or sequences having at least 75% identical to nucleotides 36 to 975 of SEQ ID NO:4 or to nucleotides 1 to 705 of SEQ ID NO:11, wherein the polynucleotide encodes a polypeptide that induces oocyte activation.

The specification indicates that the nucleotide sequence of clone PT32 cDNA (1413 nucleotides) has been identified, and the nucleotides 36-975 of open reading frame (ORF) of this clone encodes a protein 313 amino acids with a molecular mass of 31,966 Da, and PT32 was found to have two PY motifs and 12 proline-rich self-repeating motifs (YGXPPXG) in its C-terminal half (page 64, paragraph [0169]); and the injection of rPT32 into cytoplasm of bovine oocytes yield rates of oocyte activation that were similar to the rate of activation injected with perinuclear theca extracts (Table 1, pages 64-78).

However, the specification does not describe a genus of variants for a sequence that hybridizes to the sequence of SEQ ID NO:4 or 11 and encodes a polypeptide having the activity of inducing oocyte activation; and sequences having at least 75% identical to nucleotides 36 to 975 of SEQ ID NO:4 or to nucleotides 1 to 705 of SEQ ID NO:11. A species of polynucleotide (e.g., nucleotides 36-975 of SEQ ID NO:4 or nucleotides 1-705 of SEQ ID NO:11) does not provide original descriptive support for a genus of nucleotide sequences that hybridize to the sequence of SEQ ID NO:4 or 11 and encode a polypeptide having the activity of inducing oocyte activation, or a sequence having at least 75% identical to nucleotides 36 to 975 of SEQ ID NO:4 or to nucleotides 1 to 705 of SEQ ID NO:11 and encoding a functional polypeptide. The variant for the polynucleotides do not meet the written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Applicants have described specific examples of nucleotides 36 to 975 of SEQ ID NO:4 or to nucleotides 1 to 705 of SEQ ID NO:11, however, a genus of variants for nucleotide sequence that hybridizes to the sequence of SEQ ID NO:4 or 11 under a cited hybridization condition and encodes a polypeptide having the activity of inducing oocyte activation; and nucleotide sequences having at least 75% identical to nucleotides 36 to

975 of SEQ ID NO:4 or to nucleotides 1 to 705 of SEQ ID NO:11 and encoding a functional polypeptide have not been described nor disclosed.

The skilled artisan cannot envision all the contemplated compounds based upon the general suggestion of functional characteristics of polynucleotides. The detailed structure must be taught, therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of preparation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of making. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF'S were found unpatentable due to lack of written description for the broad class.

Therefore, only those embodiments described and disclosed meet the written description requirement and not the full breadth of the claim meets the written description provision of 35 USC 1 12, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 9 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 48 recite the limitation "a conservative variant thereof " in lines 2-3. There is insufficient antecedent basis for this limitation in the claim because claim 73 recites a nucleotide sequence of SEQ ID NO:4 and 11, which encode the polypeptide of SEQ ID NO:5 and 12, respectively, the claim does not recites a nucleotide sequence, which encodes a conservative variant of SEQ ID NO:5 or 12.

Claim Objections

7. Claim 10 and 74 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

8. Claims 8, 9, 11-15, 48, 53, 60-62, 65-67 and 73 are rejected, and claims 10 and 74 are objected to.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D. CMK
Patent Examiner

CMK
August 26, 2004

Jon P. Weber, Ph.D.
Primary Examiner